IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF VIRGINIA
ALEXANDRIA DIVISION

PFIZER INC., *et al.*, Plaintiffs, v. TIGER PHARMACEUTICALS, LLC, Defendant.	Civil Action No. 1:14-cv-1501 (AJT/TRJ)

SUPPLEMENTAL DECLARATION OF CRAIG ECKHARDT, PH.D.

I, Craig Eckhardt, Ph.D., declare as follows:

1. I am the same Craig Eckhardt, Ph.D., who submitted a declaration, dated February 4, 2015 (D.I. 44-8 to 44-13, "Feb. 4 Declaration"), in support of Tiger's Opening Claim Construction Brief in this case. I incorporate my previous declaration and supporting exhibits by reference as if fully set forth herein.

2. I have been asked by Tiger to respond to Pfizer's Opening Claim Construction Brief dated February 4, 2015 (D.I. 46) and the declaration of Leonard J. Chyall, Ph.D., dated February 4, 2015, filed with Pfizer's Opening Brief (D.I. 46-1). In forming the opinions expressed in this declaration, I have relied on my knowledge, education, training and experience, in addition to these materials (D.I. 46 to 46-6), as well as the other documents cited in and attached to this declaration and my prior declaration.[1]

I. "DOFETILIDE POLYMORPH P[#] WHICH IS CHARACTERIZED BY DSC IN WHICH IT EXHIBITS AN ENDOTHERMIC THERMAL EVENT AT ABOUT [ ]° C"

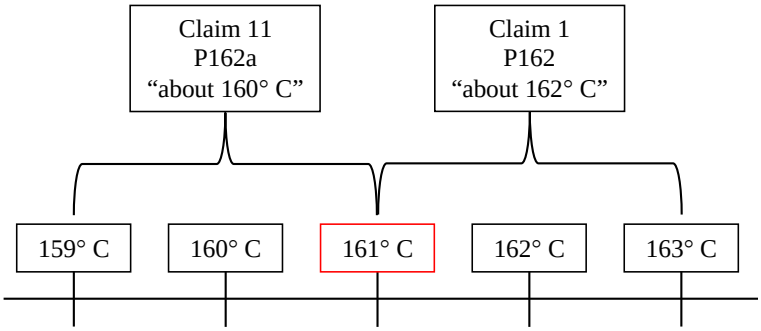
3. As an initial matter, I note that Dr. Chyall has not set forth an opinion as to how a person of ordinary skill in the art would have interpreted claim 1 of the '363 patent. I reserve my right to provide additional opinions should Dr. Chyall: (1) opine how a person of ordinary skill in the art would have interpreted claim 1; or (2) dispute the opinions expressed in my first declaration.

4. I maintain my opinion that a person of ordinary skill in the art would understand the term "dofetilide polymorph P[#] which is characterized by DSC in which it exhibits an endothermic thermal event at about [ ]° C" in claims 1, 11 and 17 to mean that (1) DSC must be used to distinguish the claimed form of dofetilide and that (2) the term "about" would encompass a range of ± 0.3° C.

[1] As my Feb. 4 Declaration had five exhibits attached to it, I have begun numbering further exhibits with "Exhibit 6."

A. Requirement That DSC Distinguish the Claimed Form of Dofetilide

5. Pfizer argues that requiring DSC to distinguish one claimed polymorph from other polymorphic forms is "unnecessary" because "[c]laims 1, 11, and 17 of the '363 patent themselves distinguish dofetilide polymorphs P162, P162a, and P143 based on DSC analyses that characterize each polymorph." (D.I. 46 at 12.) However, Pfizer's logic is internally inconsistent. If Pfizer's interpretation of the term "about [ ]° C" to mean "within 1° C of [ ]° C" were used, then a substantially pure dofetilide polymorph that exhibits an endothermic thermal event at 161° C would read on both claim 1 as P162 and claim 11 as P162a as shown below:



Thus, Pfizer's construction of the term "about [ ]° C" would not, in my opinion, "distinguish dofetilide polymorphs P162, P162a, and P143 based on DSC analyses that characterize each polymorph." (D.I. 46 at 12.) Where a ± 1° C range is used, one of ordinary skill in the art would be unable to distinguish between the claimed polymorphs P162 and P162a.

6. Requiring DSC to distinguish one claimed polymorph from other polymorphic forms is indeed necessary precisely because the specification of the '363 patent instructs a person of ordinary skill in the art that there is no other way to distinguish the claimed dofetilide polymorphs P162 and P162a from each other and from the prior art dofetilide polymorph P162b. The '363 patent explains the significance of the DSC peaks recited in the claims, stating that:

> Dofetilide polymorphs P162a and P162b have similar PXRD patterns and IR spectra, but different DSC characteristics, to dofetilide polymorph P162.

(D.I. 44-9, '363 patent at col. 2, ll. 56-61.) A person of ordinary skill would have concluded, therefore, that the differences in the DSC peaks are necessary to distinguishing the claimed dofetilide polymorphs P162 and P162a from each other and from the prior art dofetilide polymorph P162b.

B. "About [ ]° C"

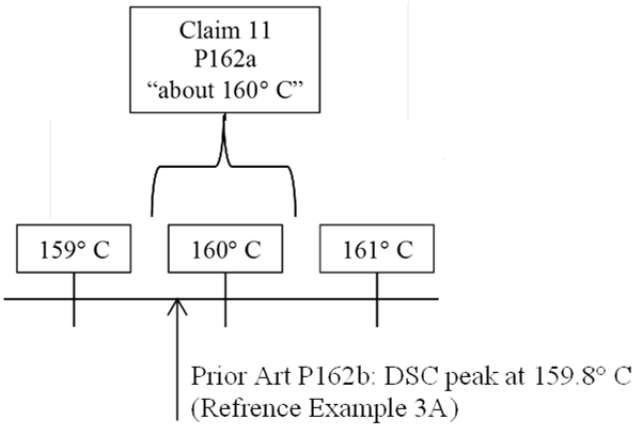
7. Pfizer and Dr. Chyall cite to no evidence in support of their belief that a person of ordinary skill in the art would have understood the term "about" to encompass a range of temperatures within one degree of the claimed temperature.

8. At most, Dr. Chyall provides two statements purportedly based on his personal experiences. Dr. Chyall's conclusory statements that, in his personal experience, "DSC measurements conducted on different samples of the same material in the same laboratory may differ by ± 0.5 °C" and that "DSC analyses conducted in different laboratories will be in agreement to ± 1 °C" is anecdotal evidence at best and not based in science. (D.I. 46-1 at ¶ 25.) It is always possible to observe extreme variations in DSC through improper techniques and from failure to routinely or properly calibrate a DSC. In my experience, I have seen some poorly designed and poorly executed DSC analyses with even more than a ± 1 °C discrepancy. Properly designed and executed DSC analyses, however, are at least within a range of ± 0.3º C.

9. First, the specification of the '363 patent states that "DSC was performed using a Perkin Elmer DSC-7 machine." (D.I. 44-9, '363 patent at col 14, ll. 19-20.) The manual for the Perkin Elmer DSC-7 machine states that the machine has a temperature precision of ± 0.1 °C and a temperature accuracy of ± 0.1 °C. (Ex. 6, Perkin Elmer DSC-7 Manual, at "Specifications".) Furthermore, a person of ordinary skill in the art would have expected that such an instrument would have been well calibrated. The identification of such a precise and accurate instrument in the specification of the '363 patent would give further weight that a person of ordinary skill

would understand the term "about" to encompass a range of no more than ± 0.3º C. If anything, the '363 patent's identification of a Perkin Elmer DSC-7 would support an even narrower view of the term "about," not a broader one.

10. Second, even a range as broad as ± 0.3º C would allow claim 11 to read on dofetilide polymorphs that were known at the time the patent application was filed. For example, the specification of the '363 patent states that the EP-A-0245997 patent publication provided what was "essentially dofetilide polymorph . . . P162b." dofetilide polymorph P162b was known in the prior art. (D.I. 44-9, '363 patent at col. 1, ll. 50-54.) I understand that the EP-A-0245997 qualifies as prior art because it was published in April 1992, which is more than one year before the October 9, 1998 filing date of the '363 patent. According to the '363 patent, Reference Example 3A is dofetilide polymorph P162b. (Id. at col. 8, ll. 47-57.) Table 2 states the DSC peak of Reference Example 3A is 159.8º C. (Id. at Table 2, col. 15.) Thus, the specification of the '363 patent itself identifies that the DSC peak of dofetilide polymorph P162b made with prior art methods is only 0.2º C away from the claimed DSC peak for the dofetilide polymorph P162a in claim 11. Thus, a person of ordinary skill in the art would have reasonably concluded the term "about" could be even narrower for claim 11 than ± 0.3º C to prevent claim 11 from reading on dofetilide polymorph P162b.



11. Third, Pfizer and Dr. Chyall cite to Michael E. Aulton, Pharmaceutics: The Science of Dosage Form Design, 238 (1988) ("Aulton") (D.I. 46-3) regarding the difference in melting point required to establish a difference in the relative stability of polymorphs. The relative stability of polymorphs, however, has nothing to do with the magnitude of uncertainty associated with a DSC measurement being able to characterize one polymorph from another. In other words, DSC measurements would be able to tell two polymorphs apart with an error range of ± 0.3º C even if no conclusions may be made as to their relative stability.

12. Aulton not only fails to support Pfizer's proposed construction of "about" to be a range of ± 1° C, Aulton contradicts Pfizer's proposed construction. For example, Aulton states there may be differences in melting point between polymorphs that are "< 1 °C." (Id. at 238.) If DSC had a variability of ± 1° C, it would be unable to distinguish polymorphs with DSC peaks that are less than one degree apart.

13. Furthermore, Aulton specifically cites the United States Pharmacopeia ("USP") as the authoritative reference with regard to thermal analysis (e.g. DSC). (Id. at 238.) As I explained in my Feb. 4, Declaration, the USP monograph regarding DSC states the temperature at which a DSC peak occurs can be determined "objectively and reproducibly, often to within a few tenths of a degree." (D.I. 44-13, United States Pharmacopeia and National Formulary (USP 23-NF 23), 1837-1838 (1995) ("USP 23").) In particular, "[m]elting point determinations by scanning calorimetry have a reproducibility with a standard deviation of about 0.2°." (Id. at 1838.) That one cannot determine the relative stability of polymorphs that differ in their melting point by less than one degree is thus irrelevant to understanding how a person of skill in the art would have understood the term "about" in the claims of the '363 patent.

14. Fourth, Pfizer and Dr. Chyall further misunderstand why a person of ordinary skill in the art would have understood the term "about" to encompass a range of ± 0.3º C. They believe it is because Table 2 of the '363 patent happens to list the DSC peak for dofetilide polymorph P143 as 144.3º C, or 0.3º C higher than the claimed temperature of 144º C of claim 17. This is incorrect, however. As I explained fully in my Feb. 4 Declaration, a person of ordinary skill in the art would have understood the term "about" to encompass a range of ± 0.3º C because (1) the USP states DSC measurements are reproducible "within a few tenths of a degree," (2) a range of ± 0.3º C is consistent with the most generous value permitted by the specification, (3) a range of ± 0.3º C allows for a clear distinction between all the claimed dofetilide polymorphs based on their DSC characteristics, and (4) a range of ± 0.3º C prevents claims 1 and 11 from reading onto the melting point of the prior art Rasmussen dofetilide polymorph's melting point of 161º C.

II. PERSON OF ORDINARY SKILL IN THE ART

15. Pfizer and Pfizer's expert, Dr. Chyall, propose a definition of a person of ordinary skill that overstates the qualifications a person of ordinary skill would have had with respect to the '363 patent. Although I disagree with Dr. Chyall's definition of a person of ordinary skill in the art, the opinions expressed in my Feb. 4 Declaration and in this declaration would be the same even if viewed from the perspective of what Pfizer considers to be one of ordinary skill in the art for the '363 patent.

* * *

I declare under penalty of perjury that the foregoing is true and correct. Executed on February 18, 2014.

Craig Eckhardt

Craig Eckhardt, Ph.D.